



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

Tuesday, November 08, 2016

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 5383-ROL
DP Barcode: D434612
Product Name: Troysan ZPT38

From: Ian Blackwell, Biologist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Through: Jenny Tao, Senior Toxicologist
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To: Jacqueline Hardy, PM 34/ Stacey Grigsby
Regulatory Management Branch
Antimicrobials Division (7510P)

Applicant: Troy Chemical Corporation

FORMULATION FROM LABEL:

<u>PC Code</u>	<u>Active Ingredient(s):</u>	<u>% by wt.</u>
088002	Zinc pyrithione	38
	<u>Other Ingredient(s):</u>	<u>62</u>
	Total:	100

I **BACKGROUND:** The Troy Chemical Corporation has submitted a complete set of six acute toxicity studies in support of the registration of their product, "Troysan ZPT38". Product Safety Labs conducted these studies.

II **RECOMMENDATIONS:**

1. Each of the six studies is acceptable.

The acute toxicity profile for File Symbol 5383-ROL is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	49931003	III	Acceptable
Acute Dermal Toxicity	49931004	III	Acceptable
Acute Inhalation Toxicity	49931005	IV	Acceptable
Primary Eye Irritation	49931006	III	Acceptable
Primary Skin Irritation	49931007	IV	Acceptable
Dermal Sensitization	49931008	Nonsensitizer	Acceptable

III **LABELING:**

Label Review System

PRODUCT ID #: 005383-00195

PRODUCT NAME: Troysan ZPT38

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Causes moderate eye irritation. Harmful if swallowed or absorbed through skin. Avoid contact with skin, eyes or clothing. Remove and wash contaminated clothing before reuse. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

First Aid:

If in eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- Call a poison control center or doctor for treatment advice.

If on skin:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.

If swallowed:

- Call a poison control center or doctor immediately for treatment advice.
- Have person sip a glass of water if able to swallow.
- Do not induce vomiting unless told to by a poison control center or doctor.
- Do not give anything to an unconscious person.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Label Created by: Ian Blackwell on 11/08/2016 Last Updated by: Ian Blackwell on 11/08/2016

The submitted label for 5383-ROL states that users of this product must wear protective eyewear, long-sleeved shirt, long pants, socks, chemical-resistant gloves and chemical resistant footwear. Based upon the Agency's Label Review Manual, these statements are not required for this product. However, Troy Chemical Company may retain these statements if they wish to do so.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Product Manager: 34

MRID No.: 49931003

Reviewer: I. Blackwell

Study Completion Date: 12/29/2015

Lab Study No.: 42131

Testing Laboratory: Product Safety Labs

Authors: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160.12): Included

Test Material: Kopthione 38% FPS. "Off-white dispersion"

Species: Sprague-Dawley derived albino rats

Weight: 151-179 g

Age: 8-11 weeks

Source: SAGE Labs

Conclusion:

1. LD₅₀ (mg/kg):

Males= Not tested

Females= 1,750 mg/kg

Combined= Not tested

2. The estimated LD₅₀ is 1,750 mg/kg

3. Tox. Category: III

Classification: Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
175	Not tested	0/1	Not tested
550	Not tested	0/2	Not tested
1,750	Not tested	1/2	Not tested
5,000	Not tested	1/1	Not tested

Observations: Hypoactivity, anogenital staining, irregular respiration, reduced fecal volume, diarrhea, hunched posture.

Gross Necropsy:

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 34

Reviewer: I. Blackwell

MRID No.: 49931004

Study Completion Date: 2/1/2016

Lab Study No.: 42132

Testing Laboratory: Product Safety Labs

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160.12): Included

Test Material: Kopthione 38% FPS. "Off-white dispersion"

Species: Sprague-Dawley derived albino rats

Weight: Males= 289-324 g

Age: 9-10 weeks

Females= 190-217 g

Source: Sage Laboratories

Summary:

1. **LD₅₀ (mg/kg):**

Males= > 2,000 mg/kg

Females= > 2,000 mg/kg

Combined= > 2,000 mg/kg

2. The estimated LD₅₀ is greater than 2,000 mg/kg.

3. **Tox. Category:**

III

Classification: Acceptable

Procedure (Deviation From §81-2):

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2,000	0/5	0/5	0/10

Observations: No abnormalities.

Gross Necropsy Findings: No abnormalities were reported.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: 34
MRID No.: 49931005

Reviewer: I. Blackwell
Study Completion Date: 2/1/2016
Lab Study No.: 42133

Testing Laboratory: Product Safety Labs
Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160.12): Included

Test Material: Kopthione 38% FPS. "Off-white dispersion"
Concentration: 2.07 mg/L

Species: Sprague-Dawley derived albino rats
Weight: Males= 277-289 g Females= 180-190 g
Age: 8-9 weeks
Source: Sage Labs

Summary:

- | | | | |
|----|---|-----------------|-----------------------------------|
| 1. | LC₅₀ (mg/L) | Males | > 2.07 |
| | | Females | > 2.07 |
| | | Combined | > 2.07 |
| 2. | The estimated LC₅₀ is greater than 2.07 mg/L. | | |
| 3. | MMAD: | 2.82 | µm |
| 4. | Toxicity Category: | IV | Classification: Acceptable |

Procedure (Deviation from §81-3):

Results:

Exposure Concentration	Reported Mortality		
	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2.07 mg/L	1/5	1/5	2/10

Chamber Atmosphere		
Dose Level	MMAD	GSD
2.07 mg/L	2.82 μm	2.58 μm

Chamber Environment	
Chamber Volume	28 liters
Airflow	60 LPM
Temperature	20-21° C
Relative Humidity	60-62%

Clinical Observations: Moist rales, hypoactivity, irregular respiration, red nasal discharge, anogenital staining, gasping.

Gross Necropsy Findings: Lungs extremely red, stomach and intestines extremely distended.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)**Product Manager:** 34**Reviewer:** I. Blackwell**MRID No.:** 49931006**Study Completion Date:** 12/29/2015**Lab Study No.:** 42134**Testing Laboratory:** Product Safety Labs**Author(s):** Carolyn Lowe, LATG**Quality Assurance (40 CFR §160.12):** Included**Test Material:** Kopthione 38% FPS. "Off-white dispersion"**Dosage:** 0.1 mL**Species:** New Zealand albino rabbit**Sex:** 3 females**Weight:** 2228 – 2609 g**Age:** 13 weeks**Source:** Robinson Services, Inc.**Summary:****1. Toxicity Category:** III**2. Classification:** Acceptable**Procedure (Deviations from §81-4):** None**Results:**

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal Opacity	0/3	3/3	3/3	0/3	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Conjunctivae								
Redness	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
Chemosis	3/3	3/3	3/3	3/3	3/3	0/3	0/3	0/3
Discharge	3/3	3/3	3/3	2/3	2/3	0/3	2/3	2/3

- - - = no observations at this point

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 34

MRID No.: 49931007

Reviewer: I. Blackwell

Study Completion Date: 12/29/2015

Lab Study No.: 42135

Testing Laboratory: Product Safety Labs

Study Director: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160.12): Included

Test Material: Kopthione 38% FPS. "Off-white dispersion"

Dosage: 0.5 mL

Species: New Zealand albino rabbit

Weight: 2344-2453 g

Age: 12 weeks

Source: Robinson Services, Inc.

Summary:

1. **Toxicity Category:** IV
2. **Classification:** Acceptable

Procedure (Deviations from §81-5): None

Results: The lab reported that there was no erythema or edema during the 72 hours of the study.

Special Comments: None

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 34

MRID No.: 49931008

Reviewer: I. Blackwell

Study Completion Date: 2/16/2016

Lab Study No.: 42136

Testing Laboratory: Product Safety Labs

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160.12): Included

Test Material: Kopthione 38% FPS. "Off-white dispersion", pH 8.82

Positive Control Material: α -Hexylcinnamaldehyde (HCA)

Species: Hartley albino guinea pig

Weight: 309-408 g

Age: "young adult"

Source: Hilltop Lab Animals

Method: Buehler Method

Summary:

1. **This Product is not a dermal sensitizer.**
2. **Classification:** Acceptable

Procedure (Deviation from §81-6): None

Procedure:

Induction: Ten males and ten females were dosed with 0.4 mL of undiluted test material using a 20 x 20 mm lint cotton patch. After 6 hours, the patches and test material were removed and the exposure site cleansed with distilled water. This procedure was repeated once a week for the following two weeks (Days 7 and 14 of the study), for a total of three induction exposures.

Challenge: Fourteen days after the third induction exposure, the test material-induced animals were challenged using the same dosing procedure with 0.4 mL of a neat solution (the Highest Non-Irritating Concentration) of the test material on a naïve spot.

Results:

Induction: Each of the twenty test subjects had scores of zero for the 24 and 48 hour inductions scores after each of the three induction treatments. The subjects has no erythema or edema.

Challenge: The lab reported that there was no erythema or edema in any of the 20 test subjects following challenge.